

UNITED STATES PATENT AND TRADEMARK OFFICE

**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

Ex parte GARRY B. TAKLE, ALLAN R. GOLDBERG, and SHAJI T. GEORGE

Appeal No. 2001-1498¹
Application No. 08/912,378

ON BRIEF

Before WINTERS, SCHEINER, and ADAMS, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the
examiner's final rejection of claims 1-16 and 33, which are all the claims pending
in the application.

Claims 1 and 9 are illustrative of the subject matter on appeal and are
reproduced below:

1. A method for delivering a nucleic acid to a bacterial cell, the
method comprising

bringing into contact the bacterial cell and a composition
comprising the nucleic acid and a macrocycle having a net
positive charge in an amount effective to enhance delivery of the
nucleic acid to the bacterial cell.

¹ This appeal is related to Appeal No. 2001-1705 (Application No. 08/616,141) accordingly we
have considered these two appeals together.

9. A composition for delivering a nucleic acid to a bacterial cell, the composition comprising

the nucleic acid mixed with a macrocycle having a net positive charge selected from the group consisting of natural porphyrins, natural phthalocyanins, synthetic porphyrins, synthetic phthalocyanins, and conjugates thereof, in an amount effective to enhance delivery of the nucleic acid to the bacterial cell,

wherein the nucleic acid is a nucleic acid to be delivered to a bacterial cell, wherein the nucleic acid is ionically bound to the macrocycle.

We also note that claims 4 and 12 further limit the macrocycle of claims 1 and 9, respectively, to porphyrin. In addition, claim 13 further limits the composition of claim 9 by requiring that the composition be made by mixing a plurality of the porphyrin and a plurality of the nucleic acid in a ratio resulting in all of the plurality of the nucleic acid binding to the plurality of the porphyrin.

The references relied upon by the examiner are:

Takle	WO 95/27480	Oct. 19, 1995
Yuan	WO 95/24489	Sept. 14, 1995
Sessler	WO 96/21665	Jul. 18, 1996
George	WO 96/21731	Jul. 18, 1996

Ernst-L. Winnacker (Winnacker), From Genes to Clones Introduction to Gene Technology 487-490 (Horst Ibelgauf, trans., VCH 1987)

Gibbs et al. (Gibbs), "Interaction of Porphyrin and Metalloporphyrins with Nucleic Acids," Seminars in Hematology, Vol. 26, No. 2, pp. 77-85 (1989)

Ortigao, et al. (Ortigao), "Solid-phase Introduction and Intracellular Photoinduced Reaction of a Water-soluble Meso-tetracarboxyporphine Conjugated to an Antisense Oligodeoxynucleotide," Biochimie, Vol. 75, pp. 29-34 (1993)

Kobayashi et al. (Kobayashi), "Reversal of Drug Sensitivity in Multidrug-Resistant Tumor Cells by an MDR1 (PGY1) Ribozyme," Cancer Res., Vol. 34, p. 1271-1275 (1994)

Merchat et al. (Merchat), "Meso-substituted Cationic Porphyrins as Efficient Photosensitizers of Gram-positive and Gram-negative Bacteria," J. Photochemistry and Photoiology B: Biology, Vol. 32, pp. 153-157 (1996)

GROUND OF REJECTION

Claims 9-12 and 14 stand rejected under 35 U.S.C. § 102(b) as anticipated by Gibbs.

Claim 13 stands rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Gibbs.

Claims 1-4 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Takle, George or Sessler in view of Merchat.

Claims 4-8 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Takle, George or Sessler in view of Merchat and further in view of Ortigao, Yuan, Kobayashi and Winnacker.

Claims 15, 16 and 33 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Gibbs or Ortigao in view of Yuan, Kobayashi and Winnacker.

We reverse.

DISCUSSION

THE REJECTION UNDER 35 U.S.C. § 102:

According to the examiner (Answer, page 6), Gibbs "teaches compositions comprising calf thymus DNA, ... ionically bound and intercalated by synthetic porphyrins...." In addition, the examiner finds (Answer, page 16), "[a]ny nucleic acid or nucleic acid derivative can be used in the disclosed porphyrin compositions and delivered to bacterial cells using the disclosed method."

However, as set forth in Gechter v. Davidson, 116 F.3d 1454, 1457, 43 USPQ2d 1030, 1032 (Fed. Cir. 1997), “[u]nder 35 U.S.C. Section 102, every limitation of a claim must identically appear in a single prior art reference for it to anticipate the claim.” In this regard, the examiner failed to establish that the macrocycle component of the composition is present in an amount effective to enhance delivery of the nucleic acid to bacterial cells, as is required by the claimed invention.

In our opinion, the examiner’s suggestion that any nucleic acid or derivative thereof can be used together with porphyrin for delivery to bacterial cells is not a reasonable basis to shift the burden to appellants to demonstrate that the effective amount required by the claimed invention is the same as that in the prior art. We are mindful that there is a line of cases represented by In re Swinehart, 439 F.2d 210, 212, 169 USPQ 226, 229 (CCPA 1971) which indicates that where an examiner has reason to believe that a functional limitation asserted to be critical for establishing novelty in the claimed subject matter may, in fact, be an inherent characteristic of the prior art, the examiner possesses the authority to require an applicant to prove that the subject matter shown to be in the prior art does not possess the characteristic relied on. Nevertheless, before an applicant can be put to this burdensome task, the examiner must provide some evidence or scientific reasoning to establish the reasonableness of the examiner's belief that the functional limitation is an inherent characteristic of the prior art. In the case before us, no such evidence or reasoning has been set forward.

Accordingly, we reverse the rejection of claims 9-12 and 14 under 35 U.S.C. § 102(b) as anticipated by Gibbs.

THE REJECTION UNDER 35 U.S.C. §§ 102(b)/103:

The examiner maintains his rejection of claim 13 over Gibbs utilizing the same evidence set forth in the rejection under 35 U.S.C. § 102(b). Claim 13, however, ultimately depends from claim 9. Therefore, for the reasons set forth, supra, we reverse the rejection of claim 13 under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103 as obvious over Gibbs.

THE REJECTIONS UNDER 35 U.S.C. § 103:

Claims 1-4:

According to the examiner (Answer, page 7-8), Takle, “discloses methods of delivery of microparticles bearing the porphyrin heme and external guide sequences (EGS) into liver cells”; George, “discloses methods of delivery of microparticles bearing the porphyrin heme and external guide sequences (EGS) into liver cells”; and Sessler, “discloses delivery of any negatively charged substances, including antisense oligonucleotides, with the porphyrin derivative turcasin, into cells.” However, the examiner recognizes (Answer, page 8) that “Takle, George and Sessler do not teach methods of delivery of compositions to bacterial cells.” To make up for this deficiency, the examiner relies on Merchat to teach “the delivery of porphyrin compounds to bacterial cells.” Id.

In response, appellants argue (Brief, page 9), that the external guide sequences of Takle and George are not directly bound to the porphyrin as is

required by appellants' claimed invention. Of the three primary references separately relied upon by the examiner, only Sessler discloses conjugates of nucleic acid molecules and porphyrins for delivery into eukaryotic cells. Id. In this regard, appellants argue (Brief, page 10), "the fact that porphyrins were known to enter bacterial cells ... does not provide any reasonable expectation of success for the delivery of a combination of porphyrin and nucleic acid where the porphyrin may be masked."

We remind the examiner that "[t]he consistent criterion for determination of obviousness is whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have a reasonable likelihood of success, viewed in the light of the prior art." In re Dow Chemical Co. 837 F.2d 469, 473, 5 USPQ2d 1529, 1531 (Fed. Cir. 1988).

On this record, the examiner relies on Takle, George and Sessler teaching that delivery of nucleic acids into cells, wherein uptake by porphyrin increases the delivery of nucleic acids, to provide the reason to utilize a porphyrin-nucleic acid composition to deliver nucleic acid into bacterial cells. However, as appellants point out (Brief, page 10), "[t]here is ... no suggestion in any of the publications (or within the general knowledge of those of ordinary skill in the art) to even attempt to deliver a conjugate of porphyrin and nucleic acid to a bacterial cell."

Therefore, it is our opinion, the combination of references relied upon by the examiner fails to suggest or provide a reasonable expectation of success in carrying out the claimed invention. Accordingly, we reverse the rejection of

claims 1-4 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Takle, George or Sessler in view of Merchat.

Claims 4-8:

According to the examiner (Answer, page 10), Takle, George, and Sessler, taken separately, and further in view of Merchat, fail to teach the various limitations of the dependent claims. To make up for these deficiencies the examiner relies on Ortigao, Yuan, Kobayashi and Winnacker. Ortigao, Yuan, Kobayashi and Winnacker, however, fail to make up for the deficiency in the combination of Takle, George, and Sessler, taken separately, and further in view of Merchat, see supra. Therefore, for the reasons given above, we reverse the rejection of claims 4-8 stand rejected under 35 U.S.C. § 103 as being unpatentable over any one of Takle, George or Sessler in view of Merchat and further in view of Ortigao, Yuan, Kobayashi and Winnacker.

Claims 15, 16 and 33:

According to the examiner (Answer, page 13), “Gibbs, teaches a composition comprising a nucleic acid mixed with a macrocycle, which is a porphyrin, that has a net positive charge, wherein the nucleic acid is ionically bound to the macrocycle.” In addition, the examiner finds (id.), “Ortigao teaches a composition comprising a nucleic acid covalently bound to a porphyrin in a 1:1 ratio that is efficiently transported into rat epithelial cells in culture. Ortigao teaches that a synergism of oligonucleotide and porphyrin substituent in uptake into cells.” The examiner, however, recognizes (id.), “[n]either Gibbs or Ortigao teach an external guide sequence (EGS) that cleaves an RNA molecule that

confers drug resistance to bacteria; wherein the EGS comprises as [sic] least one modified nucleotide; or an EGS that cleaves an RA molecule required for viability of the cell.”

To make up for the deficiencies in Gibbs or Ortigao, the examiner relies on Yuan, Kobayashi and Winnacker. According to the examiner (Answer, page 14), “[o]ne of ordinary skill in the art would have been motivated to make such a composition comprising EGS that target drug resistance in order to render drug-resistant bacteria in hospitals susceptible to killing....” Stated differently, the examiner reason combining the prior art is to have a composition for delivering a nucleic acid to a bacterial cell. The combination of references however, fails to suggest or even attempt to deliver a conjugate of porphyrin and nucleic acid to a bacterial cell. Prima facie obviousness based on a combination of references requires that the prior art provide “a reason, suggestion, or motivation to lead an inventor to combine those references.” Pro-Mold and Tool Co. v. Great Lakes Plastics Inc., 75 F.3d 1568, 1573, 37 USPQ2d 1626, 1629 (Fed. Cir. 1996).

[E]vidence of a suggestion, teaching, or motivation to combine may flow from the prior art references themselves, the knowledge of one of ordinary skill in the art, or, in some cases, from the nature of the problem to be solved. . . . The range of sources available, however, does not diminish the requirement for actual evidence. That is, the showing must be clear and particular.

In re Dembiczak, 175 F.3d 994, 999, 50 USPQ2d 1614, 1617 (Fed. Cir. 1999) (citations omitted). Therefore, it is our opinion, the combination of references relied upon by the examiner fails to suggest or provide a reasonable expectation of success in carrying out the claimed invention. Accordingly, we reverse the

rejection of claims 15, 16 and 33 under 35 U.S.C. § 103 as being unpatentable over any one of Gibbs or Ortigao in view of Yuan, Kobayashi and Winnacker.

REVERSED

Sherman D. Winters)	
Administrative Patent Judge)	
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)	
)	BOARD OF PATENT
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